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Application of 40% Trichloroacetic Acid in the Treatment for Recurrent Genital Herpes

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ABSTRACT

Background: Genital herpes is one of the common sexually transmitted diseases affect more than 400,000,000 individuals worldwide. The disease characterized by relapse and remission courses and caused by herpes simplex virus (HSV) type 2. However, satisfactory curative agents are still unavailable.
Objectives: This study intends to evaluate the benefit of 40% Trichloroacetic acid (TCA) in the management of recurrent genital herpes lesions of the external male genitalia and to detect the recurrence rate during this therapeutic regimen.
Materials and methods: The study extended between 1998 to 2017 and totally, 175 patients with active disease were treated by oral administration of acyclovir 400mg 5 times per day for 5 days. Only 99 patients were followed up for one year and enrolled in the study. After 2 weeks, the recurrent cases were subjected to the chemical peeling using topical application of 40% TCA at the site of reactivation.
Results: The most affected age group was 40-50 years (n=45, 45.45%). The neck of the penis was the most affected site (n=56, 56.57%). Forty patients had only one recurrence during a one-year follow-up after treatment with 40% TCA.
Conclusion: This study approved the clinical effectiveness of the topical application of 40% TCA in reducing the recurrence rate of the genital herpes lesions. We recommend using this chemical peeling method in the treatment of patients with genital herpes.

Keywords: Recurrent genital herpes simplex virus (RGHSV), Herpes Simplex Virus (HSV), Trichloroacetic acid (TCA), Acyclovir (ACV).

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INTRODUCTION

Herpes lesions have been described since antiquity and herpes derives from the Greek word to creep or crawl. It was included in the references reported by physicians Hippocrates and Galenn, approximately 2000 years ago regarding the spreading nature of herpetic skin lesions [1]. Genital herpes caused by HSV and is one of the common sexually transmitted diseases. The disease characterized by lifetime recurrent courses of remission and relapse. According to the HSV protein coat, it divides into HSV types 1 and 2. The virus belongs to DNA viruses.

Orolabial herpes caused by HSV type 1, while, genital herpes is caused by HSV type 2. Despite each virus is a distinct entity, both of them have some antigenic components, such that antibodies that react to one virus may "neutralize" the other type. The determination of the specific type depends on HSV culture and PCR [2–5]. However, PCR is unable to differentiate the active from the latent state of the virus [6].

Direct contact is the way of the HSV transmission from individual to individual. The infection begins once the virus contacting the disrupted skin or mucosa. The incubation period of the HSV ranged from 2 to12 days where the virus replicates in the epidermis and dermis and causing inflammation and cellular destruction. Then the virus becomes latent in the sensory ganglia and reactivates from time to time with either recurrent ulcerative lesions or asymptomatic shedding. No vectors are involved in the transmission of the virus. Herpes is an endemic disease because it is characterized by lifetime

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recurrent courses of remission and relapse, latent infection, and asymptomatic shedding. Symptomatic virus lesions are more liable for transmission because they have higher viral titers. HSV transmission from men to women is more efficient than from women to men owing to high recurrence rate, and hence infectivity, in men [6].

At puberty HSV type 2 antibodies start to form, and this correlates with the sexual activity. The lifetime seroprevalence ranged from 20 to 80% [7]. There are many factors affecting the severity and recurrence rate including gender, viral type, prior immunity to the heterologous or autologous virus, and immune status of the individual [7–10]. A prodromal feature for 2 hours-2 days is the characteristic of recurrent genital herpes and these include pain, burning at the site of eruption, and tenderness. HSV in the perianal region which may extend to the rectum is common in homosexual men [11]. The choice of the treatment depends on the recurrence rate either no treatment for infrequent attacks or local or oral antiviral drugs for more severe forms. Long-term suppressive therapy, which can be continued for up to one year, is also an option. The third option is the supportive treatment for up to one year, this kind may reduce the recurrence rate [12, 13].

Trichloroacetic acid (TCA) is one of the caustic agents that use in the cauterization of warts in general as well as in genitalia. Even though it has long been traditionally prescribed for this case, the efficacy of this medication in the cure of genital warts has been evaluated in only a few series in cases of human papillomavirus [14–16]. Review of literature concerning treatment HSV patients in Iraq, revealed scarce publications, therefore this retrospective study intends to investigate the application of TCA chemical peeling in the management of genital herpes lesions at Al-Muthanna governorate/ Iraq.

MATERIALS AND METHODS

This retrospective study approved by the scientific committee of the Al-Hussein Teaching Hospital in Sammawah city/Iraq. The current study covered the period from October 1998 till October 2017. Patients with more than three recurrences of genital ulcers each year of the penis were enrolled in the present study. There were 99 men aged between 20 and 65 years with a mean age of 39.27 years ±8.81. All HSV patients were diagnosed based on clinical signs (recurrent groups of vesicles with a burning sensation at penis) because of the shortage of virology tests in Iraq due to the economic sanction and continuous war that destroyed all the infrastructural facilities even in teaching hospitals. After clinical examination, all patients with active disease were treated with a whole course of ACV 400 mg 5 times a day for 5 days. The patients were followed-up after two weeks, to re-examine, if the ulcers had been dried up completely, then a 40%TCA was applied to where the ulcers appear by using small sticks at the clinic. All the treated patients returned back every month or when a new lesion appears in the penile area. Moreover, at any time during the period of follow-up, if the patient comes with a new episode the treatment would be repeated in the same way as the first.

The data for every patient regarding the age, site of the lesions, and whether there was recurrence following treatment or not and the number of recurrences during the one-year follow-up were recorded. The age of the patients was divided into 5 groups, 20-30, 30-40, 40-50, 50-60, and $\geq$ 60 years. Figure 1 showed one of our cases who treated by application of 40% TCA to the lesion.

The data were analyzed using IBM SPSS version 24 (Statistical Package for the Social Sciences). The results presented as numbers and percentages in tables.

RESULTS

Out of 175 patients with recurrent genital herpes ulcers, 76 were excluded from this study because they were lost to follow-up. The remaining 99 was included in the study. The majority of our patients affected by genital herpes were in age groups 30-40 and 40-50 year Table 1.

The frequencies of the infection according to the location of the lesions on the penile site were 14%, 56% and 30% at glans, the neck, and the shaft respectively Table 2.

Regarding the recurrence rate following the treatment with 40% TCA of recurrent genital herpes, there were 40(40.40%) patients had one recurrence Table 3.

Apart from mild pain, and hypo-pigmentation during the application of this method, there were no other complications.

DISCUSSION

During the period of international blockade on our country (Iraq) and the lack of medicines sufficiently, we were using a TCA solution to treat warts, and it became clear to us at that time that some patients who had a recurrent genital herpes infection had recovered, or the period of recurrence of the disease decreased, and from this moment we began researching. We applied the TCA solution prepared at the pharmacy to induced white frosting with areas of erythema. This was done for every patient very carefully by the author. We need

Table 1. Shows the age groups of 99 patients.

Age groups	Frequency	Percentage
20-30	13	13.13%
30-40	37	37.37%
40-50	45	45.45%
50-60	3	3.03%
Above 60	1	1.01 %
Total	99	100

Table 2. The frequency of the lesion locations on the penis in 99 patients.

Sites of the lesions	Frequency	Percentage
Glans	13	13.13%
Shaft	30	30.30%
Neck	56	56.57%
Total	99	100

Table 3. The number of recurrences following application of 40% TCA during 1-year follow-up of 99 patients.

Number of recurrences	Frequency	Percentage
One	40(%)	40.40
Two	24(%)	24.25
Three	15(%)	15.15
Four	20(%)	20.20
Total	99	100

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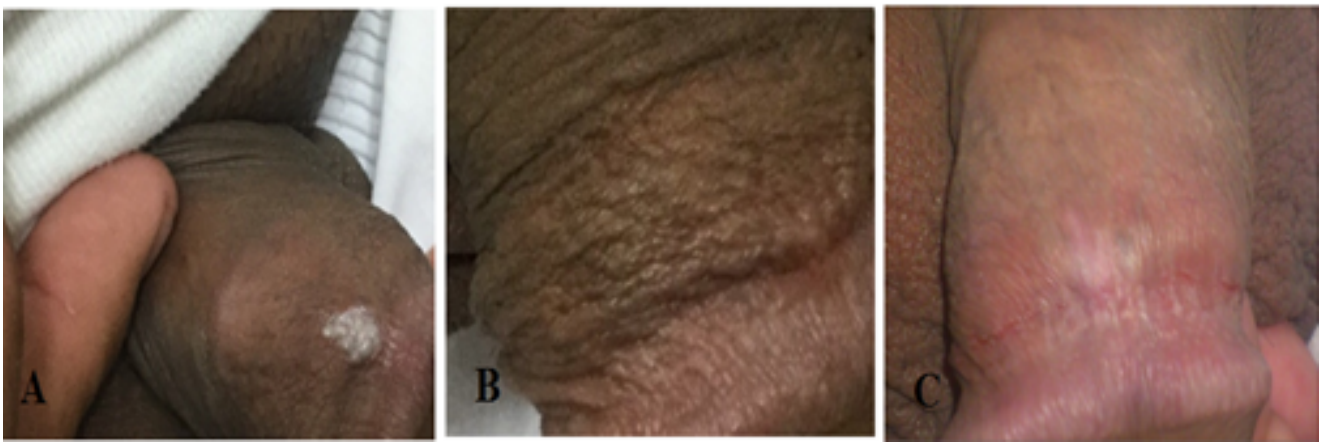

Figure 1. A. The lesions on the penis for the first time of presentation, B & C. The lesion appearance after one month and one year of application of 40% TCA to the lesion respectively.

to peel the full-thickness epidermal layers to reach the papillary dermis and that why using 40% TCA. This peel will result in full exfoliation of the epidermis, with tiny hypopigmentation, with no scaring. Later on, this drug was used for patients with genital herpes and all patients were followed for one year. The first patients came with multiple ulcers, these lesions disappeared after the removal of warts by TCA.

HSV infections may lead to the development of the chronic recurrent invasive disease. Therefore, it is mandatory to evaluate the entire external infected male genital organs to exclude the existence of any related lesions. In the present study, all patients underwent an entire clinical examination and from totally, 175 treated patients, only 99 patients were followed-up until the end of this study that extended between 1998 to 2017. There are different therapeutic modalities have been used in the treatment of HSV infections. One of the most essential shortcomings of all these methods is that none of them is 100% successful. It means that there is no cure for herpes, but medication is available to reduce symptoms and make it less about spread to a sex partner [17] The recurrence and relapse of the lesions are seen in the following- up period and necessitate additional therapeutic intermediations. The efficacy of different therapeutic regimens with success rates has been varied and the recurrence is the main drawback fate. According to the WHO protocol of treatment for GHSV [18], the following regimens were used,

1. ACV 400 mg or 800 mg orally three times/day for 5 days.
2. 500 mg Valaciclovir per-oral tow times/day for 3 days.
3. 250 mg Famciclovir tow times/day for 5 days .

Despite the above medications used for genital herpes, there are only a few advantages with few adverse effects if one compares them with no treatment. In addition, there are small differences in advantages and adverse effects between the various drugs and doses.

TCA is a caustic agent and causes cell necrosis. In the current study, all patients with active disease were treated by oral administration of ACV 400mg 5 times per day for 5 days and they were followed-up for recurrent lesions. After 2 weeks, all recurrent cases that were subjected to the chemical peeling using topical application of 40% TCA at the site of recurrent were revealed healing. However, there are variations in the percentages of the healed patients according to treatment regime and recurrences rate was 40.40%, 24.24%, 15.15% and 20.20% for first, second, third and fourth-time treatment respectively. However, the infected individual may try also to reduce the risk of spread of infection to others by regular use of condoms and by avoiding sexual contact during a reactivation episode. Virus shedding and therefore spread of HSV can also be reduced during treatment with ACV, valaciclovir, and famciclovir, either for acute disease or as prophylactic therapy [13]. In addition, the recurrent herpes genitals, improvement has been demonstrated with topical ACV but seems less impressive than that obtained by oral administration and in some studies has been ineffective. In this study, the chemical peeling of the infected area by 40% TCA revealed variable results. However, a high percentage of patients 40.40% were revealed complete healing without recurrence at the first of the treatment, while 24.24%, 15.15% and 20.20% of patients were healed at the second, third and fourth time of treatment respectively. We tried to find similar research for comparison with this research, but we have not found it yet.

In prior surveys of 3142 subjects with genital herpes reported that the mean ages of the initial attack is 31 years for males and only 4% were >50 years when they developed the first attack [19]. The mean age of our patients was 39.27 years ±8.81 which was lower than the reported mean age in the prior survey. While it's consistent with a survey regarding the affected individuals above the age of 50 years.

The limitation of the current study was it didn't study the efficiency of 40% TCA in the management of genital herpes concerning the patient age, site of the lesion and the number of recurrences. Moreover, the study didn't remove the placebo effect of the current procedure. Anyhow, this method can be used for the treatment of this nauseated condition owing to its ability to reduce the recurrence rate of the condition, and, simple, and safe procedure.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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